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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,228	11/14/2003	Luigi Grasso	MOR-0251	4529

23377 7590 01/25/2007

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,228	GRASSO ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-138* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants election with traverse of the invention of Group I and the species of anthracene. After review and reconsideration, the Election Restriction Requirement and Election of Species Requirement is withdrawn, and the following Election Requirement is made:

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 26-31, 69-61, drawn to a recombinant myeloma cell comprising a polynucleotide sequence encoding a dominant negative mismatch repair protein and a recombinant, hypermutable mammalian expression cell comprising a dominant negative mismatch repair gene, classified in class 435, subclass 325.

II. Claims 32-40 and 49-58, drawn to a method for producing mammalian expression cells that produce high titers of high affinity Ab from in vitro immunized Ig producing cells comprising cloning Ig genes from a hybridoma into a mammalian expression cell wherein said expression cells express a dominant negative allele of a mismatch repair gene, classified in class 435, subclass 455.

III. Claims 41-48, drawn to a method for producing mammalian expression cells that produce high titer high affinity Ab comprising cloning Ig genes from hybridoma cells expressing a dominant negative allele of a mismatch repair gene into a mammalian expression cell, classified in class 435, subclass 455.

IV. Claims 62-80, and claims 135 and 136, in part, drawn to a method for producing hybridoma cells that produce high affinity antibodies from in vitro immunized Ig producing cells and a method for producing hybridoma cells that produce high affinity antibodies from in vitro immunized Ig producing cells, both method comprising incubating parental hybridoma cells in the presence of at least one chemical inhibitor of mismatch repair, thereby forming hypermutated hybridoma cells, classified in class 435, subclasses 441 and 449. Claims 135 and 136 will be examined with this group to the extent that they read on claims 62 and 73.

V. Claims 81-90, and claims 135 and 136, in part, drawn to a method for producing mammalian expression cells that produce high-affinity antibodies from in vitro

immunized Ig producing cells comprising cloning Ig-genes from hybridomas into a mammalian expression cells and incubating said expression cells in the presence of at least one chemical inhibitor of mismatch repair, classified in class 435, subclasses 441 and 449. Claims 135 and 136 will be examined with this group to the extent that they read on claim 81

VI. Claims 91-101, and claims 135 and 136, in part, drawn to a method for producing mammalian expression cells that produce high titers of high affinity antibodies to a selected antigen from in vitro immunized Ig-producing cells comprising incubating hybridoma cells in the presence of at least one chemical inhibitor of mismatch repair to form hypermutated hybridoma cells and cloning Ig genes from said hypermutated hybridoma cells into a mammalian expression cell, classified in class 435, subclasses 441 and 455. Claims 135 and 136 will be examined with this group to the extent that they read on claim 91.

VII. Claims 102-106, drawn to a method for producing hybridoma cells that produce high affinity antibodies from in vitro immunized Ig-producing cells in high titers comprising combining donor cells comprising Ig-producing cells with an immunogenic antigen in vitro wherein said donor cells are naturally deficient in mismatch repair, classified in class 435, subclass 449.

VIII. Claims 107-113, drawn to a method for producing hybridoma cells that produce high affinity antibodies from in vitro immunized Ig-producing cells in high titers comprising combining Ig-producing cells with an immunogenic antigen in vitro and fusing said Ig producing cells with myeloma cells which are naturally deficient in mismatch repair, classified in class 435, subclass 449.

IX. Claims 114-123, and claims 135 and 136, in part, drawn to a method for producing mammalian expression cells that produce high-affinity Ab in high titers from in vitro immunized Ig producing cells comprising combining donor Ig-producing cells which are naturally deficient in mismatch repair with myeloma cells and cloning Ig genes from the resulting hypermutated hybridoma into a mammalian expression cell , classified in class 435, subclass 455. Claims 135

and 136 will be examined with this group to the extent that they read on claim 117.

X. Claims 124-133, and claims 135 and 136, in part, drawn to a method for producing mammalian expression cells that produce high-affinity Ab in high titers from in vitro immunized Ig producing cells comprising combining donor Ig-producing cells with myeloma cells which are naturally efficient in mismatch repair and cloning Ig genes from the resulting hypermutated hybridoma into a mammalian expression cell, classified in class 435, subclass 455. Claims 135 and 136 will be examined with this group to the extent that they read on claim 127.

XI. Claim 134, drawn to a method for the in vitro production of antigen-specific Ig-producing cells comprising isolating donor cells from an animal, treating said cells with L-Leucyl-Leucine methyl ester, incubating said donor cells with immunogenic antigen in vitro at 25-37 degrees in a medium supplemented with 5-15% serum and a growth promoting cytokine for 4 days, followed by washing of the cells in medium and further culturing in a medium supplemented with 5-15% serum form an additional 8 days thereby stimulating the production of antigen-specific immunoglobulin producing cells, classified in class 435, subclass 374.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II-VI, VIII and X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the cells of Group I can be use in a process for affinity maturation of a non-antibody binding partner, such as a synthetic polypeptide or ligand which binds to a receptor.

Inventions XI and II-X are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant

case, the combination as claimed does not require the particulars of the subcombination as claimed because the combination does not require the presence of the dominant negative mismatch repair allele, or the use of a chemical inhibitor of mismatch repair. The subcombination has separate utility such as the production of high affinity antibodies from the in vitro Ig-immunized antibodies of invention XI.

Each of Inventions II-X are distinct in their requirement for the dominant negative allele of a mismatch repair gene in the Ig-producing cell, the myeloma cell or the expression cell, versus the inhibition or mismatch repair in a hybridoma cell or in the expression cell, or the use of a naturally mismatch repair deficient donor cell for the Ig producing cell or for the myeloma cell. Thus all of the subcombinations are distinct in the particular requirements of each method in the induction of mutations.

The examiner has required restriction between combination and subcombination inventions. Where applicant elects a subcombination, and claims thereto are subsequently found allowable, any claim(s) depending from or otherwise requiring all the limitations of the allowable subcombination will be examined for patentability in accordance with 37 CFR 1.104. See MPEP § 821.04(a). Applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Claims 1-25, 137 and 138 link(s) inventions III and VII-X. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 1-25. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104. Claims that require all the limitations of an allowable linking claim will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier.

Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the

limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. In re Ziegler, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA1971). See also MPEP § 804.01.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions require a different field of search (see MPEP § 808.02), restriction for examination purposes as indicated is proper.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen A. Canella, Ph.D.
1/20/2007

KAREN A. CANELLA PH.D
PRIMARY EXAMINER